From Research
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Herbstreith&Fox

Pectins in Preventive Nutrition and Therapy

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Pectins are natural structural elements of the primary cell wall and the middle lamella of all higher land plants. Its physiological functionalities in plants are connecting and armouring cell structures and influencing the water household. Pectins mainly consist of the partial methyl esters of polygalacturonic acid and their sodium, potassium, calcium and ammonium salts.
Pectin is considered as a soluble dietary fibre. High methoxyl pectin is described in the United States Pharmacopeia and in general in the Austrian "Arzneimittelbuch".
Since a long time the beneficial physiological effects of pectins in human are studied and well-known.
The apple diet of Heisler (1803) and Moro (1929) is one of the most famous application of pectins to treat the inconsciousness of the gut. The phrase "an apple a day keeps the doctor away" can be reducted to the relatively high pectin content of apples.

Isolated pectins are said to have an influence on

- cholesterol, lipoprotein and bile acid metabolisms
- arteriosclerosi
- blood glucose level after a carbohydrate rich meal (diabetes mellitus type II)
- binding of heavy metals and their radionuclides
- weight reduction
- gastric diseases
- hemostasis and wound healing

In oriental medicinal herbs medicines additional influences are documented. According to Yamada (1996) herbal extracts contain substances with both low and high molecular weight.
Pharmacological activities have been observed in fraction with high molecular weights from boiled water extracts of the medicinal herbs. Of the high molecular weight substances, various pharmacological activities have been observed in pectic polysaccharides and pectins.
These activities are summarized by Yamada (1996) in table 1.

Table 1

Pharmacological activity of pectins isolated from plants containing medicinal herbs

Immunostimulating activity

- Complement activating activity
- Mitogenic activity
- Fc receptor up-regulation on macrophages (enhancing activity of immune complex clearance)
- Stimulation of macrophage phagocytosis

Anti-ulcer activity
Anti-metastasis activity
Anti-nephritis activity and anti-nephrosis activity
Hypoglycemic activity
Cholesterol decreasing effect

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Applications: Vaccine for typhoid fever
Drug delivery (arabinogalactan)

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Most of these immunological or anti-metastasis activities are linked to special defined parts of pectic substances like Rhamnose-rich regions, Galactan side chains, 0-acetylated pectins or encymatically or chemically degraded pectic substances. For further information to these special kind of therapeutic effects of pectins we want to refer to Yamada (1996).
In this treatise we want to concentrate mainly on the influence of pectins on serum cholesterol, serum lipids and blood glucose level as well as on some further prophylactic effects where unmodified pectins are already used.

Cholesterol and lipoprotein metabolism

Pectin and serum cholesterol is a very serious studied application. In table 2 the most important studies were summarized by Behall and Reiser in 1986. In the cited 16 studies it is significantly demonstrated that pectins have a serum cholesterol lowering effect. The diets were either controlled or self-selected without influencing the result (see table 2).

Reference	Subjects	Time	Diet	Amount Pectin g/d	Cholesterol
Keys at al. (1961)	24	3 wk	controlled	15	- 5%
Fahrenbach et al. (1965)	23	7-9 wk	?	6 - 12	0
Palmer et al. (1966)	16	4 wk	self-served	2 - 10	- 6% pn 6g or more/d
Jenkins et al. (1975)	12	4 wk	self-served	36	- 12%
Hopson et al. (1975)	3	5 wk	controlled	20 - 23	- 13%
Durrington et al. (1976)	12	3 wk	self-served	12	- 8%
Kay et al. (1977)	9	3 wk	controlled	15	- 13%
Raymond et al. (1977)	6	4 wk	controlled	2	0
Delbarre et al. (1977)	10	6 wk	controlled	6	0
Langley et al. (1977)	11	4 wk	controlled	10	Significant decrease
Jenkins et al. (1979)	5	3 wk	controlled	30	- 13%
Ginter et al. (1979)	21 11	6 wk 6 wk	self-served self-served	15 15	- 9% - 19%
Stasse-Wolthuis et. al. (1980)	62	5 wk	controlled	15	- 10%
Nakamura et al. (1982)	12	2 wk	?	9	- 10%
Judd et al. (1982)	10 10	3 wk 3 wk	self-served self-served	15 15	- 16% - 18%
Challen et al. (1983)	6	3 wk	controlled	36	- 10%
Cerda et al. (1988)	27	4 wk	self-served	15	- 15%

Table 2: Pectin and Serum Cholesterol
wk = weeks, d = day
Lit.: Behall & Reiser (1986), Cerda et al. (1988)

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But to obtain a significant decrease a minimum quantity of about 6g pectin per day has to be taken. Only one of these studies could not demonstrate this positive effect even with 6 to 12g pectin per day.

Generally it could be demonstrated that 6 to 15g pectin per day taken for 3 to 6 weeks can reduce the cholesterol level significantly by 10 to about 18%.
Additionally can be said that the intake of pectin in an amount from 2 to 6 g per day is able to stabilise a normal blood cholesterol level in healthy subjects and with that avoiding an increase of blood cholesterol.

In 1986 Herbstreith & Fox supported the study of Schuderer (1986) carried out at the Insitute of Nutrition at the University of Giessen.
For this study a high methoxyl apple pectin (Pectin Classic AU 201-USP) with a very high degree of esterification of 72-76 % was selected due to high methoxyl pectins have a higher binding capacity of lipoproteins as low methoxyl pectins because the binding mechanism is a hydrophobic interaction. This also demonstrates the advantages of high methoxyl pectins in contrast to neutral polysaccharides like guar gum which only acts by increasing the viscosity of the digestion liquor.
In this study over 21 days 20 g pectin per day were applied to subjects suffering from cholesterol levels from 260 to 340 mg per 100 ml, a LDL value from 230 +/- 50 and a HDL value of 45 +/- 20.

The subjects were either patients of the hospital, these were studied in a controlled diet, or employees of the University which were self-serving. Additional two groups were monitored without pectin but one with a cholesterol free diet and another group with a drug therapy.
In this study the controlled pectin group obtained results comparable to the drug group.
The self-serving volunteers group showed lower decreasing effects with pectin.
Eventually they did not eat the pectin that regularly as in the controlled hospital diet. The cholesterol free diet had hardly no influence on the cholesterol level (see table 3).

Value at beginning:	Total cholesterol	LDL	LDL
	300 +/- 40 mg/dl	230 +/- 50	45 +/- 20 (?)
Pectin, n = 30, controlled	- 16,7%	- 20,6%	+ 3,7%
Pectin, n = 15, self-served	- 11,8%	- 11,1%	+ 12,0%
Diet, n = 13, controlled	- 2,6%	- 5,7%	- 1,7%
Drug, n = 17, controlled	- 14,2%	- 21,0%	+ 3,9%

Tab. 3: Influence of apple-pectin on cholesterol and lipoproteins
– study Herbstreith & Fox, Schuderer (1986) –

Pectin: Classic AU 201-USP, VE° 72-76%
Dosage: 20g/d
Period: 21 days

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An additional good effect is the decrease of the dangerous low density lipoproteins (LDL), which are said to transport the cholesterol into the arterions and with that being responsible for arteriosclerosis, combined with a slight increase of the favourable high density lipoproteins transporting cholesterol out of the arterions. Combined the LDL / HDL ratio was decreased what is wanted to therapy high cholesterol levels.

The way of action how pectins can reduce the cholesterol level in the body is via the Entero-hepatic Pathway consisting of liver, small intestine and colon (see fig. 1).

Changing the diet by adding pectin a certain amount of cholesterol is bound to pectin and excreted via the colon. Only little cholesterol is back-resorpted into the liver. To produce cholesterol the liver has to use new bile acid. Knowing that the human body is producing itself 10 times more cholesterol than intaking by the daily food it is obvious that breaking down this entero-hepatic circle it is the most effective way to reduce serum cholesterol. The solubilization and swelling properties of pectins could be improved significantly in the Herbstreith & Fox product range of instant pectins. Instant pectins can be dispersed and solubilized in cold water, fruit juice or other

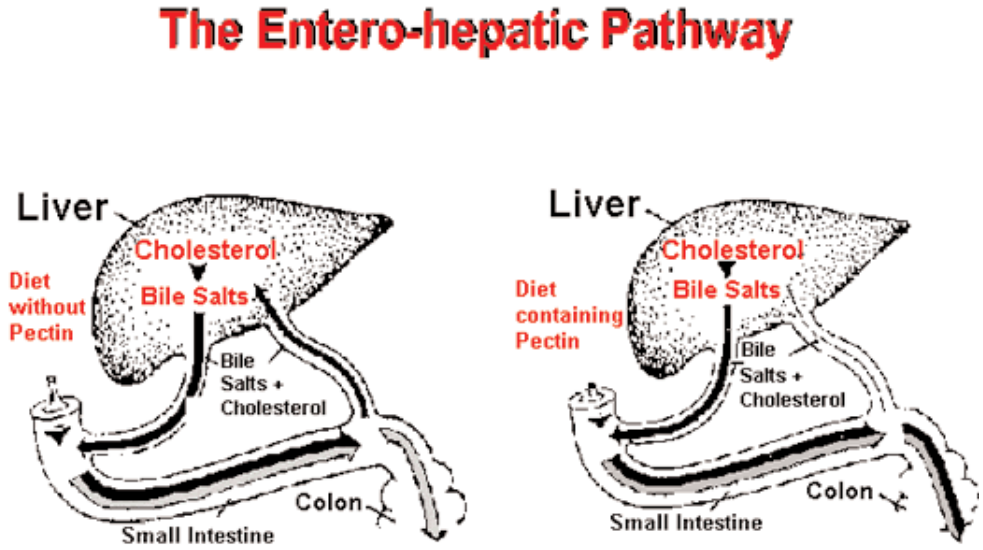

Fig. 1: Vitafood Congress 1-1997

In the case of a pectin free diet cholesterol is produced in the liver from bile salts, the cholesterol is excreted into the small intestine. Only a small quantity of the cholesterol is excreted via the colon most of it is back-resorpted into the liver and afterwards excreted again – a long lasting circle.

beverages only with slight agitation within a few minutes. This makes it much easier to prepare a pectin enriched drink.

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For industrial applications Herbstreith & Fox also offers ready to use low viscosity pectin solutions with the advantage that up to 15g of pectin can be included in half a liter fruit based beverage. The viscosity of this 3% pectin solution is about 5 mPas and with that comparable with a pulp-rich multi-vitamin juice.

An alternative to the powder pectins which are food additives from the legal point of view is a product called liquid pectin, dried, sold by our daughter company Herbafood under the trade name of Herbapekt product range.

This liquid pectin, dried, is excluded from food additives and with that a food component without any restrictions in application dosage and without an E-number what could be an advantage regarding friendly labeling.

We did also a cholesterol study with a liquid pectin, dried. This product, sold as Herbapekt SF 08 has a pectin content of 30 to 35% what is the maximum pectin content obtainable by extraction of apple pomace. Herbapekt SF 08 further consists of apple derived sugars, some fruit acids, polyphenols and minerals.

In the study, also carried out by Schuderer (1989 a), 36 g of liquid pectin, dried, was applied over a period of 21 days. The results of this study are summarized in table 4.

Parameter	Value 0 d	Value 21 d	Change 0 - 21 d
Total cholesterol	280 +/- 20	246 +/- 27	- 12.4%
HDL	54 +/- 14	55 +/- 18	+ 2.0% (n.s.)
LDL	203 +/- 19	164 +/- 25	- 19.3%
LDL / HDL-ratio	4.1 +/- 1,4 critical	3.3 +/- 1.1 positiv	- 19.5%
Apo-lipoprotein AI	158 +/- 25	157 +/- 24	- 0.4% (n.s.)
Apo-lipoprotein AII	44 +/- 8	39 +/- 10	- 11.1% (n.s.)
Apo-lipoprotein B	148 +/- 17	132 +/- 20	- 10.7%

Tab. 4: Liquid Pectin, dried*, and Cholesterol Metabolism
Dosage: 36 g/d —> 15 g pectin/d
Period: 21 days

n.s. = not significant
*tradename of Herbafood: Herbapekt SF 08, pectin content 30 - 35%

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The results are comparable to the powder pectin study with apple pectin Classic AU 201 USP mentioned before. This is not surprising because the pectin in the Herbapect SF 08 is comparable to the alcohol precipitated pectin Classic AU 201. Total cholesterol and LDL level were deminished by 12.4% resp. 19.3%. The HDL level was slightly increased and the LDL / HDL-ratio was also reduced from a critical level higher than 4.0 down to the favourable value of lower than 3.5 in average.

A good correlation to the reduced LDL level showed the apo-lipoprotein B value which was also reduced by 10,7 %. The apo-lipoprotein AI and AII fractions were not changed but these values were always within the acceptable limits.

Serum Glucose and Insulin metabolism

Behall and Reiser (1986) also summarized the studies carried out on the influence of pectins on serum glucose and insulin in man. The several studies were carried out with diabetics, insulin dependent diabetics, man suffering from gastric surgery and dumping syndrom, hypoglycemics, obese and normal subjects (see table 5).

Tab. 5: Pectin and Serum Glucose and Insulin in Man
d = diabetics n = normal subjects
g = gastric surgery n.s. = not significat
h = hypoglycemic o = obese
i = insulin dependent diabetics

Lit: Behall & Reiser, 1986

Reference	Subjects	Pectin added in g	Significant decrease from control	
			Serum glucose time interval (min.)	Serum insulin time interval (min.)
Jenkins et al. (1976)	8 d	10	30 - 90	30 - 120
Jenkins et al. (1976)	3 i	10	30 - 120	---
Jenkins et al. (1977)	13 n	10	at 15 min n.s. 30 - 90	15 - 45
Leeds et al. (1977)	5 m dumping syndrom	10,5	at 30 min improved retention of load in stomach	---
Jenkins et al. (1978)	6 d	14,5	n.s.	n.s.
Monnier et al. (1978)	6 d	9/sqm body surface	30 - 60	n.s.
Holt et al. (1979)	6 n	14.5	30 - 45	---
Labayle et al. (1980)	23 m	10 - 20	at 30 min	---
Labayle et al. (1980)	3 z	5	Hypoglycemia overted	---
Vaaler et al. (1980)	8 i	15	15 - 90	---
Poynard et al. (1980)	7 i	7	60 - 90	at 180 min
Gold et al. (1980)	6 n	10	n.s.	n.s.
Gold et al. (1980)	6 n	10	60 - 90	n.s.
Williams et al. (1980)	13 d	10	at 60 min	n.s.
Kanter et al. (1980)	5n, 6f, 5d	10 + Guar	Significant decrease in all subjects, Greatest change in obese and diabetic subjects	
Schwartz et al. (1983)	7 n	20	n.s.	---

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The applied pectin dosages vary between 10 and 20g per day. The studies were short termin studies. The analytical parameter was the significant decrease from control of serum glucose and serum insulin detectable in a defined time interval after the food intake.
In general the glucose level was decreased significantly in the time interval between 30 and 90 minutes after food intake.
The serum insulin was detected only in a few of these studies and the measured values show either a significant decrease of insulin 15 up to 180 minutes after food intake or were not significant.

We wanted to know if there is the same influence of liquid pectin, dried, on the postprandial serum glucose level as with powder pectins. The study was done in the hospital of Passau by Schuderer et al. (1989 b). Patients suffering from diabetes mellitus type II were treated with 36 g of Herbapekt SF 08 corresponding to 15 g pectin. It could be shown (see fig. 2) that the postprandial serum glucose level was much lower than in the control group due to the reduced resorption of glucose.
The serum glucose level could be kept beyond the critical value of 150 mg glucose per 100 ml serum only by dietetic means.

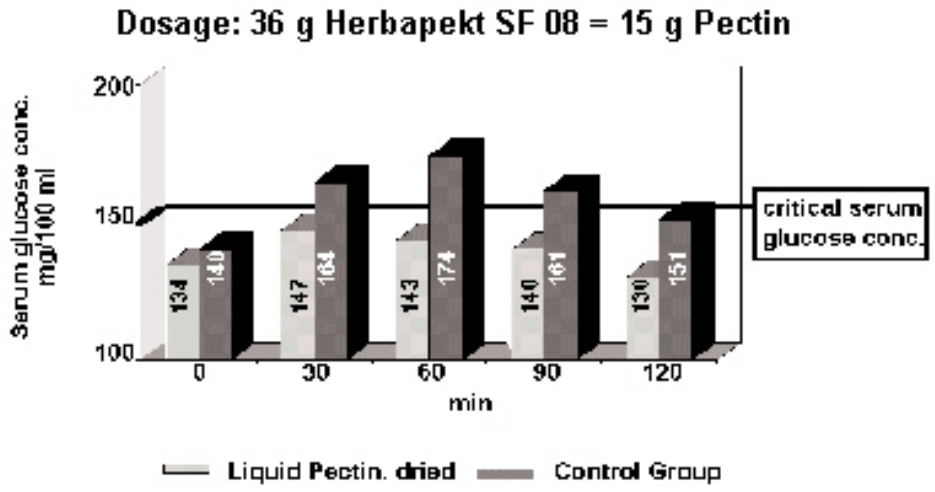

Fig. 2: Influence of liquid pectin, dried on the post prandial serum glucose concentration
Vitafood Kongress 1-97, Schuderer et al. (1989)

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A study with an amount of 24 g Herbapekt SF 08 corresponding to 10 g pectin did not show a significant reduction of serum glucose from control, probably due to the too low viscosity-increase of the digestion liquor by 10 g pectin and the higher glucose intake of the liquid pectin group compared to the control group.
But with the higher pectin intake of 15 g the increased glucose intake was more than compensated by the increased viscosity of the digestion liquor.

Weight Reduction

There are several mechanisms responsible for the weight reduction by the soluble dietary fiber pectin.

a) gel formation – gel filtration

In contrast to neutral polysaccharides pectins are able to form gels or jelly like structures in the intestines. The gel formation makes it more difficult to build up encyme-substrate complexes and with that the degredation of the food to its resorpable substances is reduced.
By a gel filtration system of the pectins food components like sugar, fats, acids or cholesterol but also endogenous metabolites like bile acids are fixed and the resorption is reduced respectively delayed.

b) unstirred water layer

The intestinal mucosa is involved in an unstirred water layer which is increased in thickness by pectins (Flourie et al. 1984).
That way the contact between the intestinal digestion encymes and the food components is deminished resulting also in a lower concentration of resorpable substances.

c) mouth-caecum-transit time

The swelling soluble dietary fibers slow down the emptying of the stomach. Holt (1979) found an increase of the emptying half time from 23 to 50 minutes by
10g of pectin. This is a very good effect for patients suffering from dumping syndrom.
But also the intestinal transit time is prolonged by the increased viscosity of the digestion liquor by the pectins. That way the feeling of satiety is prolonged.

d) reduction of the pancreatic encymes activities

By pectins the activities of pancreatic encymes are reduced. According to Isaksson (1982) and Dutta (1985) the amylase activity is reduced by 10 to 40%, the lipase activity by 40 to 80% and the trypsin activity by 15 to 80%.
To obtain these reduction 1.5g pectin were added to 100 g food resulting in an increase of the viscosity of the duodenal liquid from 30mPas to about 230mPas.
Another reason for the reduced activity is due to the binding of encymes to the hydrocolloids.

These effects together are responsible for the weight reduction by a longer feeling of satiety, a reduced degradation of food to resorpable substances and by a reduced resorption itself.

Binding and Excretion of heavy metals and their radionuclides

A special property of pectins is their ability to bind heavy metals by a complexation mechanism. This is possible because pectins are negatively charged polyelectrolytes and can bind positively charged heavy metal ions.

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The binding affinity is very high for lead, followed by barium, cadmium and strontium and decreases to earth alkali and alkali ions.
With that low methoxyl pectins are an antidote for heavy metal poisoning by an increased excretion in the stool and with that a reduced resorption.
But also heavy metals once resorpted are excreted in the urine.

This mechanism is based on oligogalacturonides degraded from pectin by microorganisms in the colon and with that resorpable into the body. This oligogalacturonides either catalyze an excretion reaction or bind itself heavy metals resulting in an excretion via urine. The way of action is not clearly understood up to now.

From Herbstreith & Fox and Sanofi-Winthrop the product Medetopekt was developed with the assistance of the Russian Institute of Biophysics and some other medicinal centers.
Medetopekt is a tablet consisting of a low methoxyl apple pectin with a special improved binding capacity for heavy metals especially for lead and some other pectin rich apple components like liquid pectin dried, apple fiber and apple powder.
The effectiveness of Medetopekt was first studied with rats. It could be shown that the excretion of lead, cadmium and strontium was improved by Medetopekt. Consequent human studies in Kiew and Minsk varified these results.

Medetopekt was tested against crude wheat fiber. In the first study the lead content in the blood was measured before and after 21 days of Medetopekt therapy. The results with crude wheat fiber were not significant. Medetopekt reduced the lead concentration from 0.48mg per liter to 0.37mg per liter by 23% (see fig. 3).

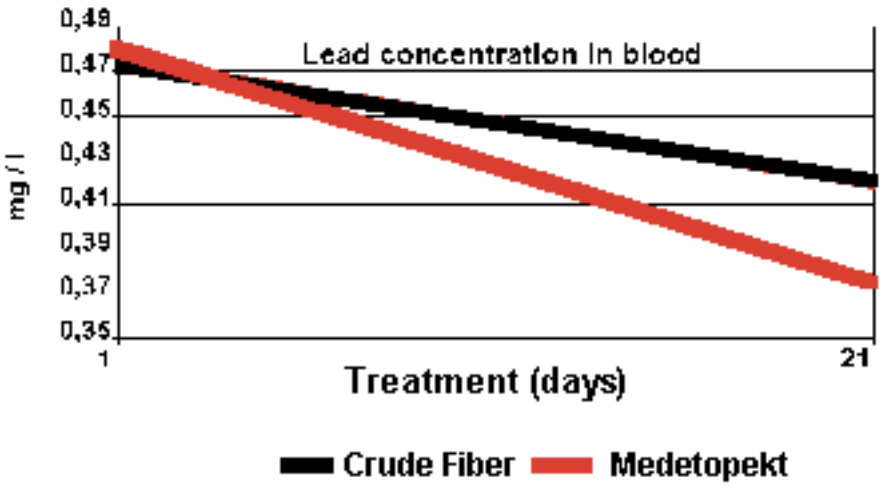

Fig. 3: Excretion of Lead - Effectiveness of Medetopekt in Comparison with Crude Fiber
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The excretion of lead via urine was significantly increased after 21 days. The volunteers left during the study their unfriendly environment. With that the lead intake and naturally occuring excretion was reduced (see fig. 4).
After some time the microorganisms probably adapted to the pectin enriched food and produced more pectin degrading encymes and with that more oligogalacturonides were formed resulting in a higher resorption of these substances and a high excretion of lead via urine at the end of the study.

A further longer study carried out in these days will show if the excretion will be further increased over a longer period.
In the strontium study the radioactive strontium was measured in the urine. The excretion of strontium was not changed significantly by crude wheat fiber but increased with Medetopekt from 0,060 Curie per liter to 0,115 Curie per liter within 21 days (visit 3, see fig. 5).

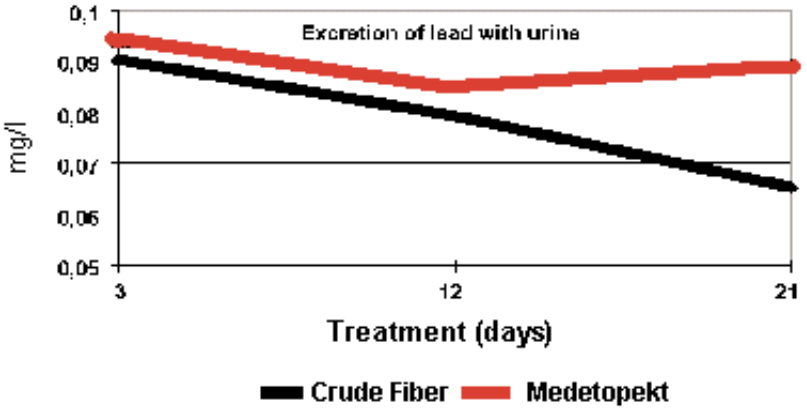

Fig. 4: Excretion of Lead - Effectiveness of Medetopekt in Comparison with Crude Fiber
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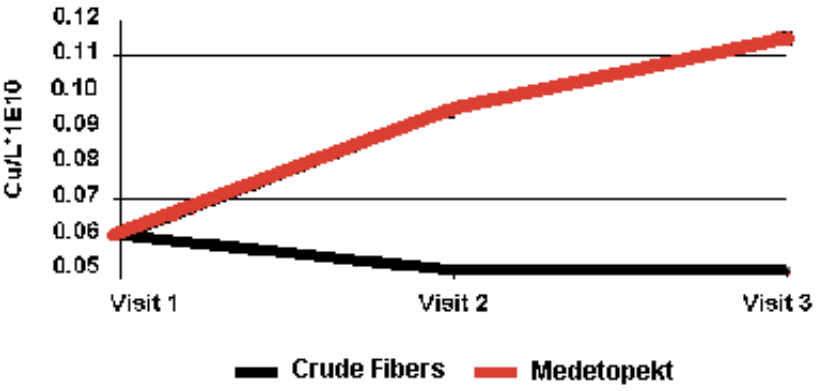

Fig. 5: Excretion of Strontium by Urine of Patients in Contaminated Regions, when Treated with Medetopekt and Crude Fibers
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Gastric deseases

Finally we can find pharmaceuticals to cure gastric deseases with pectins. In Germany for example exists the drug Diarrhoe San R, a combination of apple pectin and camilla extracts. Already grandma applied mashed apples to her children to heal their gastric disorders. The effective component is apple pectin and eventually the phenolic components. Pectin is able to bind the harmful substances irritating the gut and/or to influence the microflora supporting the growth of beneficial bacteria and suppressing diarrhoic pathogenes.
The last pictures demonstrate the diverse market of pectin containing food supplements. You can find pure apple pectin powder, mixtures of apple pectin with oat fiber, tablets composed of pectin and grapefruit fibers and so on.
Also products based on liquid pectin, dried, from the Herbapekt product range are wide spread. Mixtures of liquid pectin with apple fiber or vitamines A, C and E, minerals magnesium and calcium and lecithin have been developed.

In the United States you can find 100% apple pectin tablets. Famous products today are multi-fiber and multi-herb tablets pressed in separate tablets but sold in copackagings.
Germany is a growing market for fruit and fiber drinks. An example is a breakfast drink supplemented with vitamines A, C, E and dietary fibers wheat bran and a low viscosity pectin.

According to nutritional reports and recommendations there is a deficiency of dietary fibers in human nutrition. Today it seems to be more easy to market vitamines and minerals but these substances have not to be supplemented because they can be eaten very easily with regular food. To close the deficiency of soluble dietary fiber seems to be more difficult according to these recommendations. The components in form of suitable pectins are available and the fundamental research work is done.

This is a big challenge for developing and marketing new and attractive fiber enriched foods.

Research and Development
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